Inhibition of periodontitis progression by non-steroidal inhibitor in osteoporosis rat model : A preclinical pilot study

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Inhibition of periodontitis progression by non-steroidal inhibitor in osteoporosis rat model : A preclinical pilot study

Directed by Professor Jae-Kook Cha

The Master's Dissertation
submitted to the Department of Industrial Dentistry
and the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree of
Master's in Dental Science

Ji-Min Choi

December 2024

This certifies that the Master's Dissertation

Of Ji-Min Choi is approved.

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The Graduate School

Yonsei University

December 2024

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ABSTRACT

Inhibition of periodontitis progression by non-steroidal inhibitor in osteoporosis rat model : A preclinical pilot study

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Purpose: To investigate the effect of host modulation by increasing the systemic level of cholesterol sulfate (CS) progress of periodontitis in osteoporosis-induced rats.

Materials and Methods: Sixteen ovariectomized female Sprague-Dawley rats were included in the study, in which periodontitis was induced by applying non-resorbable suture material around the maxillary second molars on both sides for 5 weeks. During this period, the animals were fed either irosustat-mixed feed (HCS group, n = 8) or normal feed (NCS

group, $n = 8$). Block specimens were collected 5 weeks after induction of periodontitis, and histological outcomes were compared between the two groups. Statistical significance was set as $p < 0.05$.

Results: The HCS group showed significantly lower values compared to the NCS group in terms of the distance between the cemento-enamel junction (CEJ) and the apical end of junctional epithelium at proximal site (JEL; 0.36 ± 0.10 mm, 0.24 ± 0.07 mm in the NCS and HCS groups, respectively), and the distance between the CEJ and the alveolar bone crest at proximal site (BCL; 0.70 ± 0.14 mm, 0.51 ± 0.06 mm in the NCS and HCS groups, respectively). The areal percentage of the alveolar bone in the furcation area (PBF) was significantly higher in the HCS group (46.50 ± 5.14%) than in the NCS group (34.68 ± 7.14%).

Conclusions: Irosustat administration may inhibit periodontitis-induced periodontal tissue destruction by increasing systemic levels of CS.

Keywords: Animal study; Periodontitis-induced model; Cholesterol sulfate; Host modulation; Histology; Histomorphometric analysis

I. INTRODUCTION

Periodontitis is a significant infectious oral disease which causes inflammation of the periodontal attachment apparatus consisting of root cementum, alveolar bone proper and periodontal ligament (PDL) (Meyle et al., 2015; Papapanou et al., 2018; Slots et al., 2017), This inflammatory response is often followed by the progressive destruction of the periodontal supporting tissues, which can ultimately lead to tooth loss and deterioration of both masticatory function and aesthetic appearance (Papapanou et al., 2018). Treatment of periodontal disease primarily focuses on eliminating the primary causative factor, which is dental plaque (Newman et al., 1990). In some cases, this is complemented by the use of antimicrobial agents (Slots et al., 2017; Deas et al., 2016). It is widely known that the signs and symptoms associated with inflammation, such as bleeding or suppuration upon probing, gingival redness or swelling, and the formation of periodontal pockets, can be entirely resolved (Herrera et al., 2022; Graziani et al., 2017). However, it is important to note that complete regeneration of the destructed periodontal tissue is not always achievable.

To restore the periodontal attachment to its original state, several treatment options have been proposed, including guided tissue regeneration, bone graft procedures, and utilization of biologics (Nyman et al., 1987; Cortellini et al., 2015; Kao et al., 2015). While previous publications have demonstrated the efficacy of these procedures, it is well-established that the prognosis of regenerative treatment is heavily influenced by the configuration of the periodontal defect. Destruction of the alveolar ridge is typically considered irreversible unless the defect configuration presents an intrabony state (Polimeni et al., 2006). Furthermore, the situation becomes increasingly complex when patients have underlying medical conditions that impede the healing process. For example, uncontrolled diabetes can hinder oxygen delivery by disrupting peripheral vascular flow, potentially leading to unfavorable wound healing process (Guo et al., 2010), accompanied

with periodontal destruction (Liu et al., 2006). Although there is some controversy on this topic (Otomo-Corgel et al., 2012), reports indicate that the imbalance between osteoblastic and osteoclastic activities caused by osteoporosis could negatively affect periodontitis by increasing alveolar bone resorption and contributing to the atrophy of PDL (Yu et al., 2022; Huttner et al., 2009; Arioka et al., 2019).

This situation has prompted clinicians to look for the way of suppressing inflammatory destruction, which can contribute to the regeneration of periodontal attachment at compromised teeth, even in the presence of underlying systemic conditions that may impair periodontal healing process.

Since inflammation entails the activation of the host immune response, the modulation therapy targeting immunologic reaction related to periodontitis has been proposed as a viable therapeutic approach (Slots et al., 2017; Preshaw et al., 2018; Van Dyke, 2020). Various attempts have been made to utilize several candidate agents systemically, including nonsteroidal anti-inflammatory drugs (NSAIDs), submicrobial dose doxycycline (SDD), statins, probiotics, monoclonal antibodies that specifically target the receptor activator of nuclear factor kappa-B ligand, and bisphosphonates. However, despite these efforts, these agents are still regarded as insufficient for clinical application (Balta et al., 2021; Preshaw et al., 2004) or deemed inappropriate due to potential unexpected complications and side effects associated with their use (Otomo-Corgel et al., 2012; Eljaaly et al., 2023; Harirforoosh et al., 2013).

It has been reported that increasing the systemic levels of cholesterol sulfate (CS), an endogenous steroid that interferes with the activity of T-helper-17 cells, may ultimately be advantageous for controlling inflammation (Park et al., 2019; Strott et al., 2003). Additionally, CS is known to inhibit osteoclastic activity and modulate the transforming growth factor-β (TGF-β) family of proteins (Park et al., 2019). Furthermore, a recently published study demonstrated that CS suppressed osteoclastic activity by regulating the nuclear factor-kappa B (NF-κB)-involved signaling pathway (Park et al., 2023).

It has been demonstrated that the systemic level of CS could be effectively increased through the administration of a non-steroidal inhibitor of steroid sulfatase (STS inhibitor), which inactivates the enzymes responsible for catalyzing CS production (Song et al., 2024). These previous findings suggest that regulating the systemic level of CS by utilizing the STS inhibitor may serve as a promising host-modulating strategy for managing the extent of inflammatory responses in patients suffering from periodontitis, though clear evidence is still needed for the validity of this hypothesis. Consequently, the present preclinical study involving rodent models was designed to investigate how elevated systemic CS levels, achieved through STS inhibition, might affect the progression of periodontitis-induced inflammation in osteoporosis-induced rats.

II. MATERIALS AND METHODS

1. Ethical statement

The protocols for the present research, including the care and management of experimental animals, were reviewed and approved by the Animal Care and Use Committee of Yonsei Medical Center, Seoul, South Korea (approval no. 2021-0298) (Ahn et al., 2022). This study adhered to the ARRIVE guideline (Animal Research: Reporting of In Vivo Experiments) for reporting the findings of this study (Kilkenny et al., 2010).

2. Experimental animals and their housing and husbandry

Sixteen 8-week-old female Sprague-Dawley rats, weighing 300–400 g, were selected for the experiment. To induce an osteoporotic condition, the rats underwent ovariectomy performed by veterinarians at the vendor facility (Central Lab Animal, Seoul, South Korea) prior to being transported to the experimental site (Kalu et al., 1991). The animals were housed under standard laboratory conditions, with a temperature maintained at 15–20°C and humidity levels above 30%.

3. Study design and group allocation

Eight weeks after the ovariectomy, all animals were randomly allocated to one of two groups before inducing periodontitis in both maxillary second molars. Each group was assigned for different treatment protocols to assess the treatment effects under controlled conditions.

- High-CS group (n = 8): the osteoporotic rats that were administered an orally active

STS inhibitor (Irosustat; 6,7,8,9,10,11-hexahydro-6-oxobenzo[b]cyclohepta[d]pyran-3-yl ester) systemically to sustain high systemic CS levels (HCS) (Song et al., 2024).

- Normal-CS group (n = 8): the osteoporotic rats that were not administered an oral STS inhibitor (NCS).

4. Experimental protocol

The overall protocol is schematically explained in Figure 1.

4.1. Induction of periodontitis

For general anesthesia, an intraperitoneal injection of tiletamine/zolazepam (0.66 mL/kg; Zoletil 50, Virbac, Carros, France) and xylazine (0.43 mL/kg; Rompun, Elanco, Greenfield, IN, USA) was administered, along with isoflurane (Forane, Choongwae Pharmaceutical, Seoul, South Korea) inhalation via the nasal cavity. The mesial and distal interproximal contacts of both maxillary second molars were gently loosened by mild subluxation using a dental explorer. Subsequently, non-absorbable braided suture material (4-0 Black silk, Ailee, Busan, South Korea) was tied around the teeth to promote the dental plaque accumulation, leading to periodontal inflammation over a period of 5 weeks (Chew et al., 2022) (Fig. 1a).

4.2. *Fabrication of the irosustat-mixed diet*

Based on previous research that used the same experimental design (Song et al., 2024), the irosustat-mixed diet for the HCS group was made by the following method. The chow diet was first ground into a powder, and then irosustat dissolved in dimethyl sulfoxide

(253 mg/kg) was added, eventually mixing them thoroughly to create uniform pellets. The pellets were then dried for 12–15 hours, packed, and sterilized via irradiation. It was estimated that each animal would consume approximately 10 mg/kg of irosustat daily, as rats typically consume around 15g of chow per day.

4.3. *Feeding according to the group allocation*

For the 5 weeks following the induction of periodontitis, all animals were fed according to their group allocation. The HCS group received the irosustat-infused diet, while the NCS group continued to receive the standard diet without irosustat.

4.4. *Euthanasia of the experimental animals*

The rats were euthanized via exposure to excess carbon dioxide at 5 weeks after periodontitis induction. Their maxilla, including the teeth and surrounding periodontal tissues, were dissected for further histological analysis.

5. Descriptive histologic and histomorphometric analysis

After fixing the dissected maxilla in 10% neutral buffered formalin for 10 days, the specimens were dehydrated in ethanol and embedded in methacrylate. The maxillary second molars were then sectioned in the mesio-distal direction using a diamond saw (Exakt, Apparatebau, Norderstedt, Germany) and stained with hematoxylin-eosin.

Under a camera-equipped light microscope (BX-50, Olympus Optical, Tokyo, Japan), the following parameters were measured (Bhattarai et al., 2016; Garcia et al., 2015; Kajimoto et al., 2021) by a single experienced examiner (J.M.C.) who was blinded to the

group assignments (Fig. 2b and 2c):

- Junctional epithelium length (JEL, mm): the distance linearly measured from the CEJ to the apical end of junctional epithelium at the proximal area.

- Level of alveolar bone crest (BCL, mm): the distance linearly measured from the CEJ to the crestal margin of alveolar bone at the proximal area.

- Areal percentage of alveolar bone within the furcation (PBF, %): the percentage of alveolar bone area located below the furcation relative to the total area on the furcation side.

Among the parameters mentioned above, JEL and BCL were measured at both the mesial and distal sites of each tooth, and the average value of these measurements from both sides was calculated for each tooth. After collecting all the measurements from the diseased teeth in each animal, the average values for JEL, BCL, and PBF were calculated, serving as representative metrics for each animal.

6. Statistical analysis

All obtained data (mean ± standard deviation) were statistically analyzed using a computer software (SPSS version 23, IBM, New York, USA). Due to the small sample size, Mann-Whitney U test was employed for the intergroup comparison. As each animal was considered as a statistical unit, the mean values of JEL, BCL and PBF for both maxillary second molars at each rat were used for statistical analysis. Statistical significance was set as $p < 0.05$.

III. RESULTS

1. Clinical outcomes

One of the rats in the NCS group unfortunately succumbed earlier than the others due to a decline in its overall systemic health. As a consequence, the remaining animals, which included 8 rats from the HCS group and 7 rats from the NCS group, survived until the scheduled timepoint for sacrifice without exhibiting any atypical clinical signs or experiencing post-surgical complications.

2. Histological findings

In both experimental groups, remnants of the sutural material were identified in the mesial and distal interproximal spaces of the maxillary second molar. Beneath the suture material, signs of gingival inflammation were observed, which were notably more pronounced in the NCS group compared to the HCS group. Apical infiltration of junctional epithelium was observed in both groups; however, the NCS group displayed a higher abundance of inflammatory cells, characterized by their dark-purple round nuclei. A broader expanse of inflammatory connective tissue above the transseptal gingival fibers was found in the NCS group compared to the HCS group.

Additionally, an increased number of blood vessels were evident in the NCS group relative to the HCS group. Osteoclastic activity, accompanied by Howship's lacunae, was present in the alveolar bone of the NCS group, whereas such activity was scarcely observed in the HCS group. This osteoclastic activity resulted in the healthy PDL tissue in the HCS group to be located further towards the coronal portion than the NCS group at both proximal and furcation areas. Furthermore, the outer margin of the cementum in the NCS

group, particularly in the furcation area, appeared irregular and exhibited signs of excavation, while the cementum in the HCS group was comparatively smooth and well-defined. Representative histologic images are shown in Figure 3.

3. Quantitative analysis of histological images

In all measured parameters, the differences observed between the HCS and NCS groups were found to be statistically significant ($p < 0.05$). Specifically, the JEL was significantly higher in the NCS group (0.36 ± 0.10 mm) compared to the HCS group (0.24 ± 0.07 mm) ($p < 0.05$). Similarly, the attachment level, indicated by the BCL in this study, was also significantly higher in the NCS group (0.70 ± 0.14 mm) in contrast to the HCS group (0.51 ± 0.06 mm) ($p < 0.05$). Furthermore, the PBF was significantly higher in the HCS group (46.50 ± 5.14%) when compared to the NCS group (34.68 ± 7.14%) ($p < 0.05$). These findings are summarized in Figure 4.

IV. DISCUSSION

The current preclinical study aimed to histologically investigate the impact of elevated systemic levels of corticosteroids on inflammatory periodontal tissue destruction in rats induced with osteoporosis. In this study, when the rats were administered irosustat, the loss of periodontal attachment and the formation of periodontal pockets were notably less pronounced compared to the rats that did not receive the medication. Once bacterial plaque is accumulated in the gingival sulcus, an inflammatory reaction ensues, playing a crucial role in defense mechanisms (Ji et al., 2015; Jones et al., 2022). However, it simultaneously leads to the destruction of periodontal tissue, along with the infiltration of inflammatory cells into the connective tissue layer. This is followed by the PDL resorption and the apical infiltration of the junctional epithelium, ultimately resulting in a loss of periodontal attachment (Bosshardt et al., 2018; Donos et al., 2018). In the present study, the NCS group exhibited these destructive findings, while such manifestations were less prominent in the HCS group. This observation suggests that the significant increase in systemic CS levels may have contributed to the suppression of inflammation progression, thereby mitigating the extent of periodontal tissue destruction.

To manage periodontal inflammation effectively, clinicians often consider host-modulating agents such as nonsteroidal anti-inflammatory drugs (NSAIDs) or submicrobial dose doxycycline (SDD), yet robust evidence regarding their use is still needed (Preshaw et al., 2004). NSAIDs function by inhibiting the enzyme cyclooxygenase, which in turn suppress the production of metabolites derived from arachidonic acid. This suppression ultimately leads to the breakdown of inflammatory tissues, as it activates osteoclasts and stimulates the secretion of matrix metalloproteinases (Offenbacher et al., 1986). However, the routine prescription of NSAIDs can be problematic due to concerns regarding potential cardiovascular, gastrointestinal, or renal complications (Harirforoosh et al., 2013; Bindu et

al., 2020). On the other hand, SDD has been utilized as an adjunctive therapy alongside standard periodontal treatments and is recognized as a relatively safe daily medication that poses minimal risk of developing antibiotic resistance (Preshaw et al., 2004; Lee et al., 2004). Despite its proven efficacy, SDD does have limitations, particularly regarding its prescription to patients who have allergies or intolerances to tetracycline (Eljaaly et al., 2023; Mahmud et al., 2022).

In addition to NSAIDs and SDD, other therapeutic agents targeting bone metabolism have also been suggested, given that the PDL is a bone-dependent structure (Tsuchida et al., 2023). The pathological destruction of the PDL, triggered by periodontitis, is invariably accompanied by the pathological resorption of alveolar bone (Bosshardt et al., 2018). This association implies that regulating the host's systemic condition to enhance resistance against inflammatory bone destruction could play a critical role in preventing periodontal attachment loss. In this context, the efficacy of certain therapeutic agents, such as monoclonal antibodies and bisphosphonates, has been explored. However, as previously mentioned, many clinicians have expressed hesitation in prescribing these medications due to the risk of serious adverse effects, such as medication-related osteonecrosis of the jaw (Nicolatou-Galitis et al., 2019). Consequently, there has been a demand for alternative therapies. Recent studies have proposed that modulating the systemic levels of CS via agents like irosustat might serve as a promising therapeutic option (Song et al., 2024; Zaraei et al., 2019).

The irosustat used in this study functions as an inhibitor of steroid sulfatase, an enzyme responsible for hydrolyzing steroid sulfates (Reed et al., 2005). Given that CS regulate bone metabolism by modulating transforming growth factor-β family proteins, suppressing osteoclastic activity, and alleviating inflammatory responses by inhibiting T-helper-17 cells (Park et al., 2019; Strott et al., 2003), irosustat has been proposed as a promising therapeutic agent with potential efficacy in oral tissues. Supporting this, a recent study using a rodent tibial implant model demonstrated that after irosustat administration,

systemic CS levels were significantly maintained, leading to notable improvements in both bone-to-implant contact and bone density, particularly under osteoporotic conditions (Song et al., 2024). The efficacy of irosustat was confirmed not only quantitatively but also qualitatively, as the bone tissue surrounding the implant exhibited significantly higher maturation when systemic CS levels were elevated (Song et al., 2024).

The previous findings partially corroborate the results obtained from the current study, which revealed the less prominent osteoclastic activity in the HCS group compared to the NCS group, even under the osteoporotic condition which breaks the balance of bone homeostasis. Although the sole intervention received by the HCS group was the systemic administration of irosustat, the percentage of PBF in this group (averaging 46.5%) was found to be comparable to the levels previously reported after scaling and root planing procedures in rats with periodontitis at the 30-day mark (Kajimoto et al., 2021). This observation suggests that inflammation involving the furcation area, which is typically challenging to manage (Müller et al., 1999), could be effectively mitigated by elevating the systemic CS levels to a degree that could achieved through meticulous mechanical debridement.

Similarly, regarding the proximal bone level, a significant reduction in bone destruction was observed in the specimens treated with irosustat. Furthermore, the NCS group specimens exhibited a greater degree of inflammatory cell infiltration beneath the epithelium in the proximal area compared to those in the HCS group. Such inflammation would typically result in marginal gingival swelling, a condition often encountered in clinical settings. However, in the present experiment, this swelling was not observed, likely due to the presence of silk material that was maintained throughout the entire duration of the study.

The present study has several notable limitations that should be mentioned. Firstly, inflammatory cells and cytokines were not investigated in detail at the molecular or immunohistochemical levels, which limit our understanding of the underlying mechanisms

of inflammation in this study. Secondly, the present study did not compare the effect of irosustat to that of other host modulating agents, such as NSAIDs or SDDs. Thirdly, irosustat was administered solely to osteoporosis-induced animals, rather than to those that were systemically healthy, thereby limiting the generalizability of the findings. These important aspects should be further explored in future research to enhance our understanding of the effects of irosustat and to establish more comprehensive treatment strategies.

V. CONCLUSION

Pathological alveolar bone resorption and periodontal pocket formation were not evident in osteoporosis-induced rats treated with irosustat. Irosustat administration may contribute to inhibiting destruction of periodontal tissue by elevating systemic CS levels.

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FIGURES

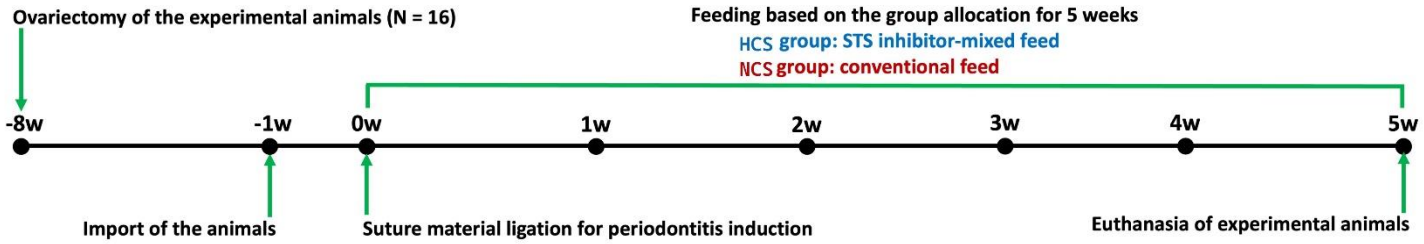

Figure 1. Overall timeline of the experiment.

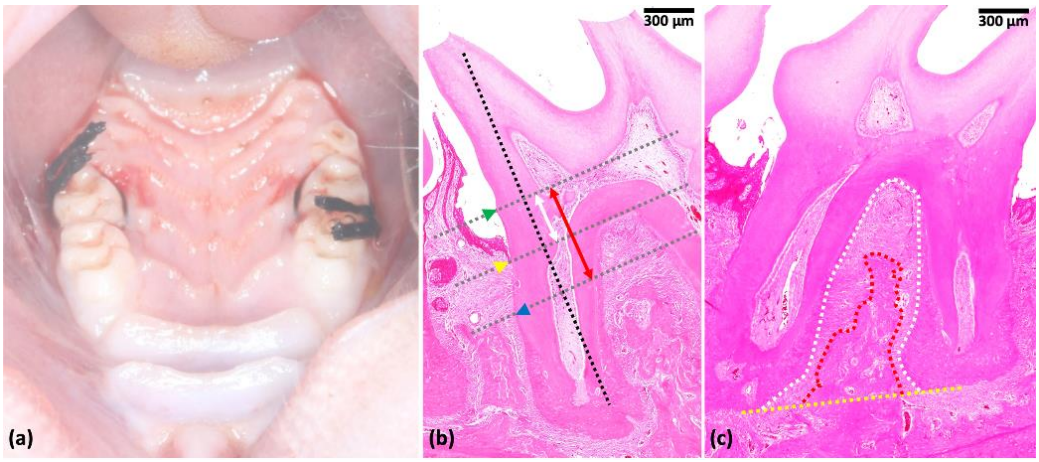

Figure 2. Clinical photograph and schematic images of histomorphometric analysis.

(a) Periodontitis induced by non-resorbable suture material was observed in both maxillary second molars. (b) The following is a schematic representation of the linear measurements for junctional epithelium length (JEL), indicated by the white double-headed arrow, and buccal clinical length (BCL), denoted by the red double-headed arrow. The green, yellow, and blue arrowheads correspond to the cementoenamel junction (CEJ), the apical end of the junctional epithelium, and the level of alveolar bone crest, respectively. Additionally, the black dotted line illustrates the long axis of the tooth, while the grey dotted lines, which are perpendicular to the black dotted line, intersect the green, yellow, and blue arrowheads. These reference lines were utilized for precise linear measurements throughout the study. (c) The methodology used for measuring the periodontal furcation bone. The yellow dotted line illustrates a straight line drawn from the apex of the mesial root cementum to the apex of the distal root cementum. Meanwhile, the white dotted line traces the contour of the root cementum that delineates the furcation area between the two roots. The red dotted line marks the outermost boundary of the alveolar bone located within the furcation region.

For the measurement of PBF, the percentage of the alveolar bone area within the furcation area (defined as the area encompassed by the red dotted and yellow dotted lines) was

calculated relative to the overall furcation area (identified as the area enclosed by the white dotted and yellow dotted lines).

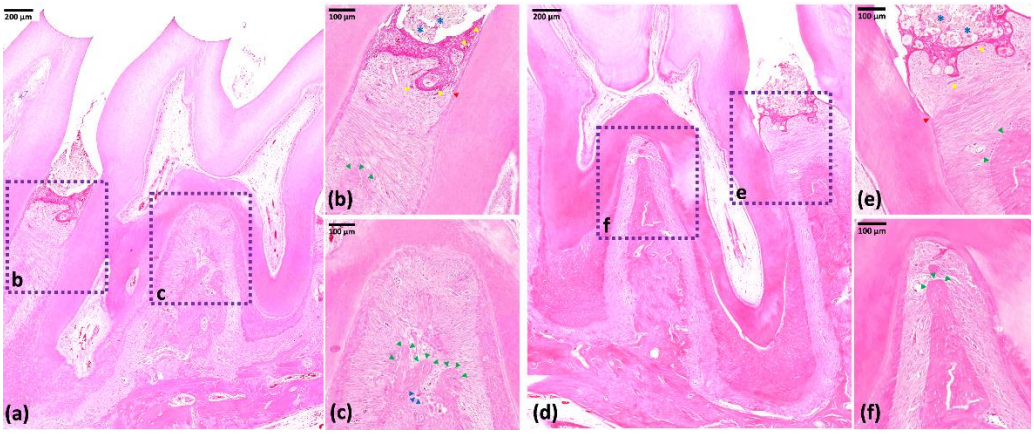

Figure 3. Representative histology of the NCS (a, b, and c) and HCS (d, e, and f) groups.

The purple-dotted boxes depicted in (a) and (d) have been enlarged and are presented in greater detail in panels (b) and (c), as well as in (e) and (f). The blue asterisks denote the suture material utilized for the induction of periodontitis. Additionally, the red, yellow, and green arrowheads correspond to specific anatomical features: the apical end of the junctional epithelium, lymphocytes, and the alveolar bone crest, respectively. (c) The blue arrowheads specifically indicate the presence of Howship's lacunae, which contain an osteoclast within them, highlighting the active remodeling processes occurring in the bone.

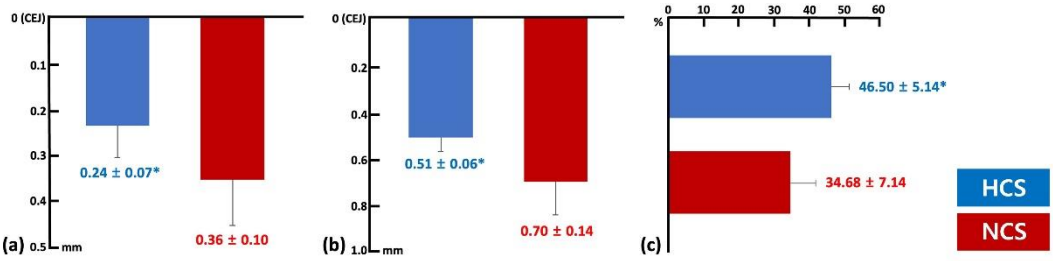

Figure 4. Results from the histomorphometric analysis.

(a) JEL, (b) BCL, and (c) PBF at both groups. Asterisks for statistical significance achieved in intergroup comparisons ($p < 0.05$).

국문요약

골다공증 쥐 모델에서 비스테로이드성 억제제 투여 여부에 따른 치주염 진행 억제 효과 비교: 전임상 예비 연구

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치주염은 치근 백악질, 치조골, 치주 인대(PDL)로 구성된 치주 부착 조직에 염증을 유발하는 감염성 구강 질환으로, 치주 조직의 파괴가 진행되면 치아 상실과 저작 기능 및 심미성 저하를 초래한다. 치주 부착을 회복하기 위해 조직 재생 유도, 뼈 이식, 생물학적 제제 사용 등의 치료법이 제안되었지만, 재생 치료의 예후는 결손 형태에 크게 좌우되며 특히 당뇨나 골다공증 등 기저 질환이 있으면 치유 과정이 더욱 어렵다. 예를 들어, 골다공증은 파골세포 활동 증가와 PDL 위축을 유도하여 치주염에 악영향을 미칠 수 있다.

이에 따라 염증을 억제하여 손상된 치주 조직을 회복하기 위해서 NSAIDs, 저용량 독시사이클린(SDD), 비스포스포네이트와 같은 면역 조절 요법이 연구되었지만. 예상치 못한 부작용과 합병증으로 인해 임상 적용에는 한계가 있었다.

최근 연구에 따르면, T-helper-17 세포의 활동을 억제하는 내인성 스테로이드인 콜레스테롤 황산염(CS) 수치를 높여 염증을 조절하고 파골세포 활동을 억제하는 데 도움이 될 수 있음을 발표하였다. 콜레스테롤 황산염

(CS)은 NF-κB 경로를 조절하여 파골세포 활동을 억제하는데, 이는 비스테로이드성 스테로이드 황산염 억제제(STS inhibitor)를 통해 체내 CS 수치를 효과적으로 높일 수 있다.

따라서, 본 연구는 스테로이드 황산화효소(STS) 억제제에 의해 증가된 콜레스테롤 황산염(CS)의 전신 수준이 골다공증이 유도된 실험쥐에서 치주질환의 염증 진행에 어떤 영향을 미치는지 조직학적으로 평가하고자 한다.

난소가 절제된 16마리의 암컷 실험 쥐를 대상으로 양쪽 상악 제 2대구치에 비흡수성 봉합사를 감아 5주간 치주염을 유발하였다. 이 기간 동안, 8마리씩 각 2그룹으로 나누어 대조군(normal-CS group; NCS)에는 일반 사료를 급여하였고, 실험군(high-CS group; HCS)에는 스테로이드 황산화효소(STS) 억제제가 혼합된 사료를 급여하였다. 5주간 치주염 유발 기간을 거친 후 두 그룹 간의 조직학적 분석을 시행하였다. 분석 지표로는 접합 상피 길이(JEL), 치조정의 높이(BCL), 그리고 치근 분지부 내 치조골 면적 비율(PBF)을 측정하였고, 각 지표의 평균 값을 계산하였다. 두 집단 간 차이는 Mann-Whitney U 검정을 통해 분석하였다. ($p < 0.05$)

조직학적 분석 결과, 두 그룹 모두 실험 부위에 봉합사가 잔존한 상태였으며, 봉합사 아래에서 NCS 그룹은 염증 세포가 더 두드러지게 관찰되었다. 이에 따라 HCS 그룹의 치주 인대(PDL) 조직은 상대적으로 치관 쪽에 더 위치하고 백악질이 매끄럽게 유지된 반면, NCS 그룹에서는 치조골 내 파골세포 활동과 흡수 공간이 뚜렷하게 나타났으며 백악질이 불규칙한 양상을 보였다. 두 그룹 간의 계측 분석 결과, 모든 지표에서 통계적으로 유의한 차이가 나타났다. 접합 상피 길이(JEL)는 HCS 그룹이 NCS 그룹에 비해 유의하게 더 낮은 값을 보였으며(NCS 그룹 0.36 ± 0.10 mm, HCS 그룹 0.24 ± 0.07 mm), 치조정 정점까지의 길이(BCL)도 유의하게 낮은 값이 나타났다

(NCS 그룹 0.70 ± 0.14 mm, HCS 그룹 0.51 ± 0.06 mm). 또한, 치근 분지부 내 치조골 면적 비율(PBF)은 HCS 그룹이 NCS 그룹보다 유의하게 높았다(HCS 그룹 46.50 ± 5.14%, NCS 그룹 34.68 ± 7.14%).

결과적으로 골다공증이 유도된 쥐에서 스테로이드 황산화효소(STS) 억제제 투여시 치조골 흡수 및 치주낭 형성이 나타나지 않았다, 따라서, 스테로이드 황산화효소(STS) 억제제 투여는 콜레스테롤 황산염(CS)의 전신 수준을 증가시켜 치주염 유발 및 치주 조직의 파괴를 억제할 수 있음을 시사한다.

핵심되는 말: 동물 실험; 치주염 유도 모델; 콜레스테롤 황산염; 조직학; 조직형태학 분석